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(71) Applicant
Imperial Chemical Industries PLC (United Kingdom),
Imperial Chemical House, Millbank, London SW1P 3JF

(72) Inventors
Christopher Richard Ayles Godfrey
Ian Thomas Dell

(74) Agent and/or Address for Service
H G H Alner,
Imperial Chemical Industries PLC, Legal Dept: Patents,
P O Box No 6, Bessemer Road, Welwyn Garden City,
Herts

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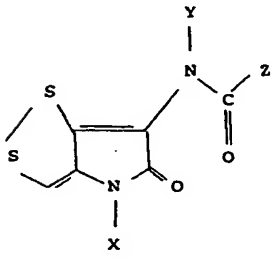
(58) Field of search
C2C

(54) Fungicidal dithiolopyrrolones

(57) Compounds of formula:



(I)

wherein X, Y and Z which may be the same or different are optionally substituted alkyl, cycloalkyl, aryl, aralkyl (especially benzyl), alkenyl or heterocyclic group; or a hydrogen atom; or wherein Z is alkoxycarbonyl; provided that when Y is a hydrogen atom X is not methyl or a hydrogen atom and when Y is methyl X is not a hydrogen atom; have fungicidal activity.

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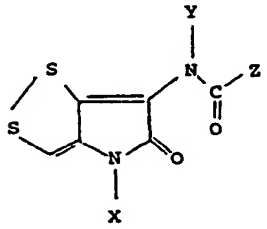
SPECIFICATION

Heterocyclic compounds

This invention relates to heterocyclic compounds useful as fungicides, to processes for preparing them, to fungicidal compositions containing them, and to methods of combating fungi, especially fungal infections in plants.

The invention provides a compound having the general formula (I):



(I)

wherein X, Y and Z, which may be the same or different, are optionally substituted alkyl, cycloalkyl, aryl, aralkyl (especially benzyl), alkenyl or heterocyclic group; or a hydrogen atom; or wherein Z is alkoxycarbonyl provided that when Y is a hydrogen atom X is not methyl or a hydrogen atom and further provided that when Y is methyl X is not a hydrogen atom. Alkyl groups can be in the form of straight or branched chains, and preferably contain 1 to 6 carbon atoms.

Several compounds having the general formula (I), wherein Y is a hydrogen atom and X is either a hydrogen atom or a methyl group, which are naturally occurring compounds, some with fungicidal activity, have been described in the literature and are not claimed as part of this invention. Examples of these compounds are thiolutin (I, $X=Z=CH_3$, $Y=H$) (see The Merck Index, ninth edition, 1976, p 1206; and references therein), holomycin (I, $X=Y=H$, $Z=CH_3$) (see The Merck Index, ninth edition, 1976, p. 620; and references therein) and the Xenorhabdin antibiotics (see CSIRO (1984) Australian Patent Applic. No. 127365). Compounds (I) derived from naturally occurring thiolutin, wherein X is a methyl group and Y is a hydrogen atom are the subject of Brit. Pat. (1956) Pub. No. 753,331. Also compound (I), wherein Y is a methyl group and both X and Z are hydrogen atoms is a naturally occurring compound with antibiotic activity (see B. Jensen, *J. Antibiotics*, 1969, *22*, 231).

Preferred alkyl groups for X, Y and Z from 1 to 6, especially 1 to 4, carbon atoms. Preferred cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. The alkyl moiety in aralkyl groups preferably contains from 1 to 4 carbon atoms.

Preferred alkenyl groups contain from 3 to 6 carbon atoms and include optionally substituted allyl, for example 3-phenylall-1-yl.

The compounds of the invention may contain chiral centres. Such compounds are generally obtained in the form of racemic mixtures. However, these and other mixtures can be separated into the individual isomers by methods known in the art, and this invention embraces such isomers.

Examples of suitable substituent groups in the benzene ring for X, Y and Z when they represent aralkyl, aralkenyl or aryl, especially benzyl, phenyallyl, or phenyl, are halogen, haloalkyl, alkyl, alkoxy (especially containing 1 to 4 carbon atoms), optionally substituted phenyl and optionally substituted phenoxy. Suitably the aryl, especially phenyl group, is unsubstituted or substituted with 1,2 or 3 ring substituents, which may be the same or different, as defined above. Examples of X, Y and Z are phenyl, 2-, 3-or 4-chlorophenyl, 2,4- or 2,6- dichlorophenyl, 2,4- or 2,6-difluorophenyl, 2-, 3- or 4-fluorophenyl, 2-, 3- or 4-bromophenyl, 2-, 3- or4-methoxyphenyl,2,4-dimethoxy-phenyl, 2-, 3- or 4-ethoxyphenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, 2-, 3- or 4-methyl-phenyl, 2-, 3- or 4-ethylphenyl, 2-, 3- or 4-trifluoro-methylphenyl, 4-phenylphenyl (4-biphenylyl), 2-chloro-4-methoxyphenyl), 2-fluoro-4-methoxyphenyl, 2-chloro-4-methylphenyl, 2-fluoro-4-methylphenyl, 4-isopropylphenyl, 2-methyl-4-chlorophenyl or 2-methyl-4-fluorophenyl.

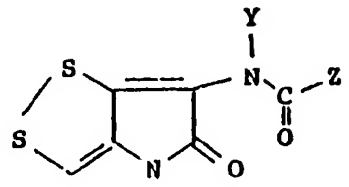
When X, Y and Z is alkyl it can be a straight or branched chain alkyl group having 1 to 6, eg. 1 to 4 carbon atoms; examples are methyl, ethyl, propyl (*n*- or *iso*-propyl) and butyl (*n*-, *sec*-, *iso*- or *t*-butyl); when X, Y and Z is alkenyl it can be allyl.

When Z is alkoxycarbonyl, preferred alkoxy carbonyl groups are C_1 to C_4 alkoxy carbonyl groups, for example methoxy or ethoxy carbonyl.

Examples of the compounds of the invention are shown in Table I. These conform to formula I and in each instance the groups X, Y and Z are as shown in the table "Ph" stands for C_6H_5 ie. for phenyl. Preferred compounds are those in which X is alkyl containing from 1 to 4 carbon

atoms; benzyl; phenyl; alkoxyphenyl wherein the alkoxy group contains from 1 to 4 carbon atoms; or allyl; or in which Y is hydrogen, methyl or phenyl; or in which Z is alkyl containing from 1 to 4 carbon atoms and optionally substituted by fluorine, chlorine or methoxy; or is methoxy or ethoxy carbonyl, or is the group 3-phenylall-1-yl.

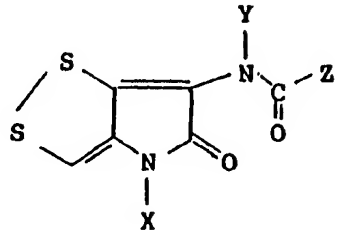
TABLE 1



X

COMPOUND NUMBERS	X	Y	Z	MELTING POINT (°C)
1	CH_3	CH_3	CF_3	214 (dec)
2	CH_3	CH_3	$CO_2C_2H_5$	85
3	CH_3	CH_3	CH_3	216
4	CH_3	CH_3	$-CH_2-CH=CH-Ph$ (t)	203-205
5	$PhCH_2-$	CH_3	$-CH_2-CH=CH-Ph$ (t)	86-89
6	$PhCH_2-$	CH_3	H	gum
7	$PhCH_2-$	H	CH_3	186
8	$PhCH_2-$	H	CF_3	214
9	$PhCH_2-$	H	H	207 (dec)
10	$PhCH_2-$	H	$CO_2C_2H_5$	115
11	$PhCH_2-$	H	CO_2CH_3	172

TABLE 1 - Contd



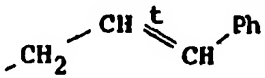
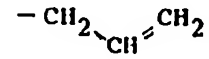
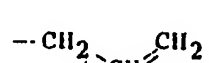
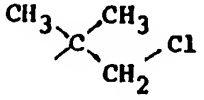
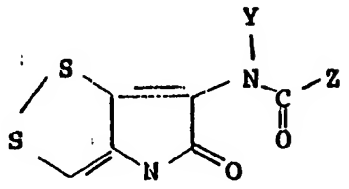
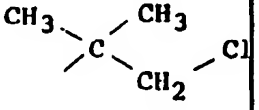
COMPOUND NUMBERS	X	Y	Z	MELTING POINT (°C)
12	$PHCH_2-$	H		225
13	$PhCH_2-$	H	CH_2OCH_3	96-98
14	$PhCH_2-$	H	$(CH_2)_4CH_3$	142-144
15	$PhCH_2-$	H	$C(CH_3)_3$	Oil
16	Ph	H	CH_3	287
17	C_2H_5	H	CH_3	223-226 (dec)
18	C_2H_5	H	CF_3	204-205
19	C_2H_5	H	H	219-223
20		H	CH_3	228-231
21		H		154-156
22	$p-CH_3O-C_6H_4-$	H	CH_3	

TABLE 1 - Contd



X

COMPOUND NUMBERS	X	Y	Z	MELTING POINT (°C)
23	i-C_3H_7	H	CH_3	
24	i-C_3H_7	CH_3	H	
25	n-C_4H_9	H	CF_3	
26	n-C_3H_7	H	$COOC_2H_5$	
27	i-C_3H_7	H	$COOCH_3$	
28	CH_3	Ph	$COOC_2H_5$	
29	CH_3	Ph	CF_3	
30	i-C_3H_7	H	CH_2OCH_3	127-130
31	i-C_3H_7	H	CF_3	129-133
32	$PhCH_2$	H		186-189

NB. Ph stands for phenyl ie. C_6H_5

The compounds of the invention having the general formula (I) can be prepared by the steps shown in *Schemes 1–4*. Throughout *Schemes 1–4* the terms X, Y and Z are as defined above; R^1, R^2 and R^3, which may be the same or different, are alkyl or aralkyl groups; R^1 and R^2 may be joined to form part of a ring; and A and B are halogen atoms or good leaving groups, which may be the same or different.

Thus, compounds of general formula (I) can be prepared by treatment of compounds of general formula (II) with an oxidising agent such as iodine, (see, for example, Schmidt and Geiger, *Annalen*, 1963, *664*, 168) or air, (see, for example, K.Hagio and N.Yoneda, *Chem. Pharm. Bull.*, 1974, *47*, 1484) in a convenient solvent such as dichloromethane (see Scheme 1).

Compounds of general formula (II), which may exist as mixtures of geometric isomers, can be prepared from compounds of general formula (III) by treatment with an alkali metal, such as lithium (when $R^1=R^2=$benzyl) in a convenient solvent, such as liquid ammonia, (see, for example, G.Büchi and G.Lukas, *J.Amer.Chem.Soc.*, 1964, *36*,5654) or by treatment with transition metal salts, such as mercury (II) acetate or copper (II) acetate (when $R^1=R^2=$^{t}Butyl; or $R^1=R^2=$alkyidene, for example methylene or isopropylidene) in a suitable solvent, such as trifluoroacetic acid, followed by treatment with hydrogen sulphide in a suitable solvent, such as dimethylformamide, (see, for example, O.Nishimura, C.Kitada and M.Fujino, *Chem.Pharm.Bull.*, 1978, *26*, 1576).

Compounds of general formula (III), which exist as mixtures of geometric isomers which can be separated, can be prepared from compounds of general formula (IV) by treatment with an acylating agent, such as acetylchloride, in the presence or absence of an acid-binding agent (such as triethylamine) in a suitable solvent, such as dichloromethane or chloroform or tetrahydrofuran, and at a convenient temperature (such as 0 to 80°C).

Compounds of general formula (IV), which exist as mixtures of geometric isomers which can be separated, can be prepared from compounds of general formula (V) by treatment with a salt of an amine YNH_2, such as ammonium acetate or anilinium acetate, with or without a convenient solvent (such as acetic acid), and at a convenient temperaure (such as 80 to 160°C).

Compounds of general formula (V), which exist as mixtures of geometric isomers which can be separated, can be prepared from compounds of type (VI)-A (which may exist as mixtures of geometric isomers and which are in equilibrium with compounds of type (VI)-B) by treatment with oxalyl chloride or bromide in the presence of an acid-binding agent (such as triethylamine) in a suitable solvent (such as dichloromethane or chloroform) and at a convenient temperature (such as −78°C to 25°C) (Scheme 2).

Alternatively, compounds of the general formula (V) can be prepared from esters of general formula (VII) by treatment with a suitable base (such as sodium hydride, lithium di-isopropylamide or lithium hexamethyldisilazide) in a suitable solvent (such as tetrahydrofuran or diethyl ether) and at a convenient temperature (−78°C to 25°C).

In addition, compounds of the general formula (V) can be prepared from compounds of general formula (IV) by hydrolysis in a suitable solvent (such as water or ethanol) in the presence of a suitable catalyst (such as hydrochloric acid) (see, for example, K.Hagio and N.Yoneda, *Chem.-Pharm.Bull*, 1974, *47*, 1484) (Scheme 1).

Esters of general formula (VII), which exist as mixtures of geometric isomers which can be separated, can be prepared from compounds of general formula (VI)-A (which may exist as mixtures of geometric isomers and which are in equilibrium with compounds of type (VI)-B) by treatment with a suitable acylating agent, such as ethyl oxalyl chloride or methyloxalyl chloride in the presence or absence of an acid-binding agent (such as triethylamine) in a suitable solvent such as dichloromethane or chloroform) and at a convenient temperature (such as 0°C).

Compounds of general formula (VI)-A (which may exist as mixtures of geometric isomers and which are in equilibrium with compounds of type (VI)-B) can be prepared from ketones of general formula (VIII) by treatment with an amine $X\text{-}NH_2$ in the presence of a dehydrating agent (such as titanium tetrachloride) in a suitable solvent (such as diethyl ether) and at a convenient temperature (−78°C to 25°C).

Ketones of general formula (VIII) can be prepared from ketones of general formula (IX) by treatment with a thiol of general formula R^1SH or R^2SH in the presence of a base (such as sodium hydride, sodium methoxide) in a suitable solvent (such as diglyme, ethanol or tetrahydrofuran) and at a convenient temperature (such as −25°C to 50°C).

Alternatively ketones of general formula (VIII) can be prepared from β-keto-esters of general formula (X) by treatment with a salt (such as lithium chloride) in a suitable solvent (such as dimethylsulphoxide) and at a convenient temperature (such as 110°C to 189°C) (see, for example, A.P.Krapcho, J.F.Weimaster, J.M.Eldridge, E.G.E.Jahngen, Jr., A.J.Lovey, W.P.Stephens, *J.Org. Chem*, 1978, *43*, 138) or by decarboxylation of β-keto-acids of general formula (XI), using standard methods as set out in the chemical literature (see, for example, H.O.House, *Modern Synthetic Methods*, 2nd edition, p.511).

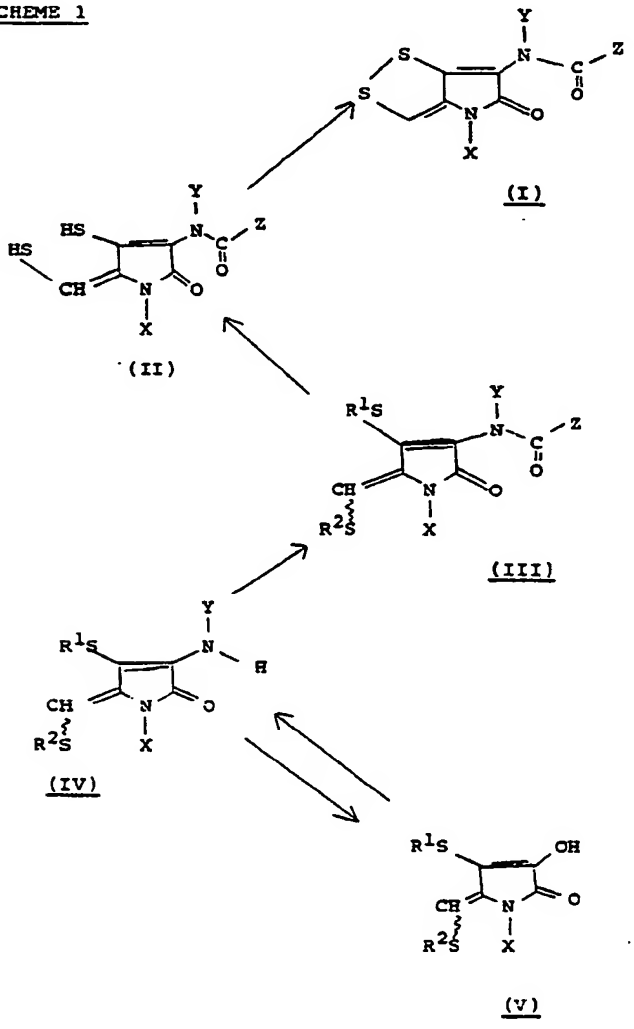
β-Keto-acids of general formula (XI) can be prepared from β-keto-esters of general formula (X) using standard methods as set out in the chemical literature (see, for example, H.O.House,

Modern Synthetic Methods, 2nd edition, P.511).

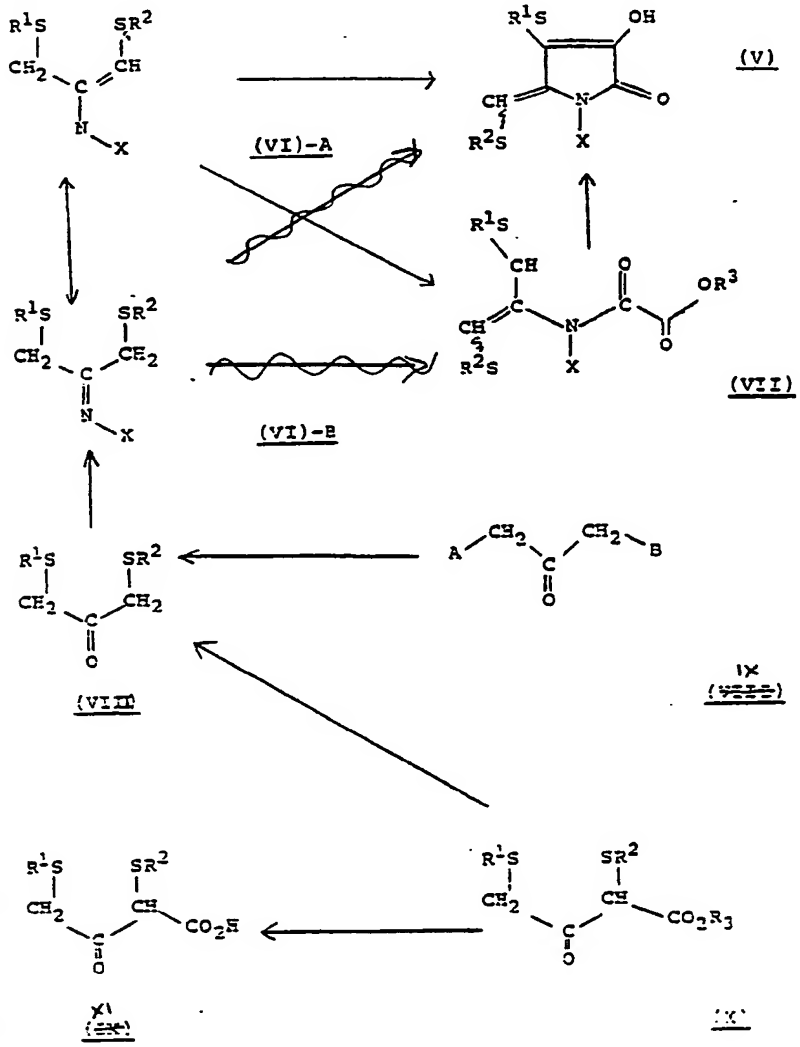
β-Keto-esters of general formula (X) can be prepared from esters of general formula (XII) or (XIII) by treatment with a base (such as sodium hydride) in a suitable solvent (such as tetrahydrofuran) and at a suitable temperature (such as 0°C to 100°C) (Scheme 3).

Compounds of general formula IV, where X=Y, which exist as mixtures of geometric isomers which can be separated, can be prepared from compounds of general formula (V), where X is an aryl substituent (such as a phenyl group) on treatment with a salt of an amine Y-NH_2, such as ammonium acetate, with or without a convenient solvent (such as acetic acid), and at a convenient temperature (such as 80°C to 160°C) (Scheme 4).

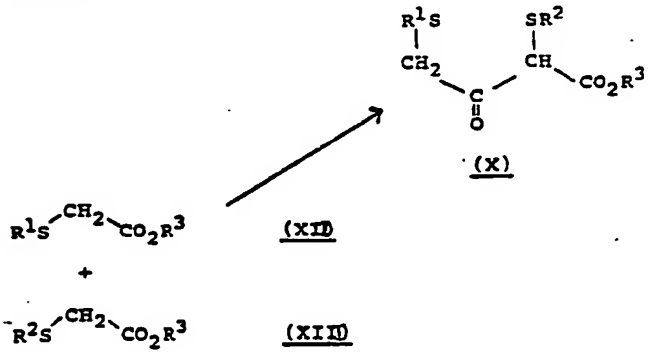
SCHEME 1



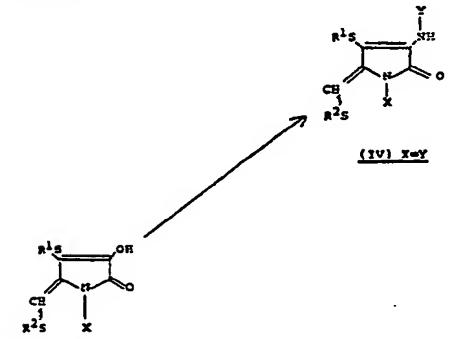
SCHEME 2



SCHEME 3



SCHEME 4



The compounds of formula I, and compositions containing them, are variously active against a wide range of fungal and bacterial diseases, particularly, for example, against:

Plasmopara viticola (downy mildew) on vines and
Phytophthora infestans (late blight) on potatoes and tomatoes and other species of *Phytophthora*
Phytophthora parasitica, Phytophthora cinnamomi,
Phytophthora palmivora and *Phytophthora capsici* on a range of commercially important crops
Pseudoperonospora cubensis on cucurbits
Peronospora tabacina on tobacco
Peronospora parasitica on cabbage
Peronospora destructor on onions
Bremia lactuca on lettuce
Pythium species on a range of commercially important crops

Other downy mildews and other fungal and bacterial diseases, for example:

Venturia inaequalis (scab) on apples
Pyricularia oryzae on rice

Cercospora arachidicola on peanuts and other *Cercospora* species.
Erysiphe graminis on barley and other powdery mildews.
Xanthomonas oryzae on rice.

Some of the compounds have also shown a broad range of activities against fungi *in vitro*. They have activity against various post-harvest diseases on fruit (eg. *Penicillium digatatum* and *italicum* on oranges and *Gloeosporium musarum* on bananas). Further some of the compounds are active as seed dressings against: *Fusarium* spp., *Septoria* spp., *Tilletia* spp. (ie. bunt, a seed borne disease of wheat), *Ustilago* spp., *Helminthosporium* spp. on cereals, *Rhizoctonia solani* on cotton and *Corticium sasakii* on rice.

The compounds can move acropetally in the plant tissue.

The compounds may be used as such for fungicidal purposes but are more conveniently formulated into compositions for such usage. The invention thus provides a fungicidal composition comprising a compound of general formula (I) as hereinbefore defined, and, optionally, a carrier or diluent.

The invention also provides a method of combating fungi, which comprises applying to a plant, to seed of a plant, or to the locus of the plant or seed, a compound, hereinbefore defined.

The compounds, can be applied in a number of ways, for example they can be applied, formulated or unformulated, directly to the foliage of a plant, or they can be applied also to bushes and trees, to seeds or to other medium in which plants, bushes or trees are growing or are to be planted, or they can be sprayed on, dusted on or applied as a cream or paste formulation, or they can be applied as a vapour; or as slow release granules. Application can be to any part of the plant, bush or tree, for example to the foliage, stems, branches or roots, or to soil surrounding the roots, or to the seed before it is planted; or to the soil generally, to paddy water or to hydroponic culture systems. The invention compounds may also be injected into plants or trees and they may also be sprayed onto vegetation using electrodynamic spraying techniques.

The term "plant" as used herein includes seedlings, bushes and trees. Furthermore, the fungicidal method of the invention includes preventative, protectant, prophylactic and eradicant treatment.

The compounds are preferably used for agricultural and horticultural purposes in the form of a composition. The type of composition used in any instance will depend upon the particular purpose envisaged.

The compositions may be in the form of dusting powders or granules comprising the active ingredient and a solid diluent or carrier, for example fillers such as kaolin, bentonite, kieselguhr, dolomite, calcium carbonate, talc, powdered magnesia, Fuller's earth, gypsum, Hewitt's earth, diatomaceous earth and China clay. Such granules can be preformed granules suitable for application to the soil without further treatment. These granules can be made either by impregnating pellets of filler with the active ingredient or by pelleting a mixture of the active ingredient and powdered filler. Compositions for dressing seed, for example, may comprise an agent (for example a mineral oil) for assisting the adhesion of the composition to the seed; alternatively the active ingredient can be formulated for seed dressing purposes using an organic solvent (for example N-methylpyrrolidone or dimethylformamide).

The compositions may also be in the form of dispersible powders, granules or grains comprising a wetting agent to facilitate the dispersion in liquids of the powder or grains which may contain also fillers and suspending agents.

The aqueous dispersions or emulsions may be prepared by dissolving the active ingredient(s) in an organic solvent optionally containing wetting, dispersing or emulsifying agent(s) and then adding the mixture to water which may also contain wetting, dispersing or emulsifying agent(s). Suitable organic solvents are ethylene dichloride, isopropyl alcohol, propylene glycol, diacetone alcohol, toluene, kerosene, methylnaphthalene, the xylenes, trichloroethylene, furfuryl alcohol, tetrahydrofurfuryl alcohol, and glycol ethers (eg. 2-ethoxyethanol and 2-butoxyethanol).

The compositions to be used as sprays may also be in the form of aerosols wherein the formulation is held in a container under pressure in the presence of a propellant, eg. fluorotrichloromethane or dichlorodifluoromethane.

The compounds can be mixed in the dry state with a pyrotechnic mixture to form a composition suitable for generating in enclosed spaces a smoke containing the compounds.

Alternatively, the compounds may be used in a micro-encapsulated form. They may also be formulated in biodegradable polymeric formulations to obtain a slow, controlled release of the active substance.

By including suitable additives, for example additives for improving the distribution, adhesive power and resistance to rain on treated surfaces, the different compositions can be better adapted for various utilities.

The compounds can be used as mixtures with fertilisers (eg. nitrogen-, potassium- or phos-

phorus-containing fertilisers). Compositions comprising only granules of fertiliser incorporating, for example coated with, the compound are preferred. Such granules suitably contain up to 25% by weight of the compound. The invention therefore also provides a fertiliser composition comprising the compound of general formula (I) or a salt or metal complex thereof.

The compositions may also be in the form of liquid preparations for use as dips or sprays which are generally aqueous dispersions or emulsions containing the active ingredient in the presence of one or more surfactants eg. wetting agent(s), dispersing agent(s), emulsifying agent(s) or suspending agent(s); or which are spray formulations of the kind suitable for use in electrodynamic spraying techniques. The foregoing agents can be cationic, anionic or non-ionic agents. Suitable cationic agents are quaternary ammonium compounds, for example cetyltrimethyl-ammonium bromide.

Suitable anionic agents are soaps, salts of aliphatic monoesters of sulphuric acid (for example sodium lauryl sulphate), and salts of sulphonated aromatic compounds (for example sodium dodecylbenzenesulphonate, sodium, calcium or ammonium lignosulphonate, butylnaphthalene sulphonate, and a mixture of sodium diisopropyl- and triisopropylnaphthalene sulphonates).

Suitable non-ionic agents are the condensation products of ethylene oxide with fatty alcohols such as oleyl or cetyl alcohol, or with alkyl phenols such as octyl- or nonyl-phenol and octylcresol. Other non-ionic agents are the partial esters derived from long chain fatty acids and hexitol anhydrides, the condensation products of the said partial esters with ethylene oxide, and the lecithins. Suitable suspending agents are hydrophilic colloids (for example polyvinylpyrrolidone and sodium carboxymethylcellulose), and the vegetable gums (for example gum acacia and gum tragacanth).

The compositions for use as aqueous dispersions or emulsions are generally supplied in the form of a concentrate containing a high proportion of the active ingredient(s), and the concentrate is to be diluted with water before use. These concentrates often should be able to withstand storage for prolonged periods and after such storage be capable of dilution with water in order to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional and electrodynamic spray equipment. The concentrates may conveniently contain up to 95%, suitably 10–85%, for example 25–60%, by weight of the active ingredient(s). These concentrates suitably contain organic acids (eg. alkaryl or aryl sulphonic acids such as xylenesulphonic acid or dodecyl benzenesulphonic acid) since the presence of such acids can increase the solubility of the active ingredient(s) in the polar solvents often used in the concentrates. The concentrates suitably contain also a high proportion of surfactants so that sufficiently stable emulsions in water can be obtained. After dilution to form aqueous preparations, such preparations may contain varying amounts of the active ingredient(s) depending upon the intended purpose, but an aqueous preparation containing 0.0005% or 0.01% to 10% by weight of active ingredient(s) may be used.

The compositions of this invention can comprise also other compound(s) having biological activity, eg. compounds having similar or complementary fungicidal, or plant growth regulating, herbicidal or insecticidal activity.

The other fungicidal compound can be, for example, one which is capable of combating ear diseases of cereals (eg. wheat) such as *Septoria, Gibberella* and *Helminthosporium* spp., seed and soil borne diseases and downy and powdery mildews on grapes and powdery mildew and scab on apple etc. These mixtures of fungicides can have a broader spectrum of activity than the compound of general formula (I) alone; further the other fungicide can have a synergistic effect on the fungicidal activity of the compound of general formula (I). Examples of the other fungicidal compound are imazalil, benomyl, carbendazim, thiophanate-methyl, captafol, captan, sulphur, triforine, dodemorph, tridemorph, pyrazophos, furalaxyl, ethirimol, tecnazene, dimethirimol, bupirimate, chlorothalonil, vinclozolin, procymidone, iprodione, metalaxyl, forsetyl-aluminium, carboxin, oxycarboxin, fenarimol, nuarimol, fenfuram, methfuroxan, nitrothal-isopropyl, triadimefon, thiabendazole, etridiazole, triadimenol, biloxazol, dithianon, binapacryl, quinomethionate, guazitine, dodine, fentin acetate, fentin hydroxide, dinocap, folpet, dichlofluanid, ditalimphos, kitazin, cycloheximide, dichlobutrazol, a dithiocarbamate, a copper compound, a mercury compound, 1-(2-cyano-2-methoxyiminoacetyl)-3-ethyl urea, fenapanil, ofurace, pro-piconazole, etaconazole and fenpropemorph.

The compounds of general formula (I) can be mixed with soil, peat or other rooting media for the protection of plants against seed-borne, soil-borne or foliar fungal diseases.

Suitable insecticides are Pirimor, Croneton, dimethoate, Metasystox and formothion.

The other plant growth regulating compound can be one which controls weeds or seedhead formation, improves the level or longevity of the plant growth regulating activity of the compounds of general formula (I), selectively controls the growth of the less desirable plants (eg. grasses) or causes the compound of general formula (I) to act faster or slower as a plant growth regulating agent. Some of these other agents will be herbicides.

Examples of suitable plant growth regulating compounds, which can display synergy in admixture, or use, with the invention compounds are the gibberellins (eg. GA_3, GA_4 or GA_7), the auxins

(eg. indoleacetic acid, indolebutyric acid, naphthoxyacetic acid or naphthylacetic acid), the cytokinins (eg. kinetin, diphenylurea, benzimidazole, benzyladenine or benzylaminopurine), phenoxyacetic acids (eg. 2,4-D or MCPA), substituted benzoic acids (eg. triiodobenzoic acid), morphactins (eg. chlorfluorecol), maleic hydrazide, glyphosate, glyphosine, long chain fatty alcohols and acids, dikegulac, fluoridamid, mefluidide, substituted quaternary ammonium and phosphonium compounds (eg. chlormequat* chlorphonium or mepiquatchloride), ethephon, carbetamide, methyl-3,6-dichloroanisate, daminozide*, asulam, abscisic acid, isopyrimol, 1-(4-chlorophenyl)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid, hydroxybenzonitriles (eg. bromoxynil), difenzoquat, benzoylprop-ethyl 3,6-dichloropicolinic acid, and tecnazene. Synergy will be most likely to occur with those of the foregoing which are quaternary ammonium compounds in particular those marks with an asterisk.

The use of the compounds of general formula (I) in conjunction with gibberellins can be useful where it is desired to reduce the plant growth regulating effects of the compounds (eg. where they are to be used as fungicides). Where the compounds are being applied to the soil surrounding the plants or to the roots of the plant, the plant growth regulating effects of the compounds may possibly be reduced by using also certain types of phenoxybenzoic acids and their derivatives.

The following Examples illustrate the invention; the temperatures are given in degrees Centigrade (°C).

EXAMPLE 1

This example illustrates the preparation of 5-(methoxyacetylamino)-4-benzyl-1,2-dithiolo[4,3-b]pyrrol-5(4H)-one (Compound No. 13 of Table I).

To a solution of sodium methoxide in dry methanol (formed by the addition of sodium (10,58g) to dry methanol (200ml)) was slowly added a solution of *t*-butylmercaptan (41,5g) in dry methanol (50ml). The resultant solution was cooled to 0°C and a solution of 1,3-dichloroacetone (29.21g) in dry methanol (50ml) was added over a period of 1 hour. The resultant mixture was stirred for a further 16 hours at room temperature and then partitioned between dichloromethane and dilute sodium hydroxide solution. The organic phase was dried over magnesium sulphate, filtered and evaporated to give a liquid. Distillation at 96°C/1mbar afforded 1,3-di(*t*-butylthio) acetone (VII, $R^1=R^2=t$-Bu—see Scheme 2) (26.42g, 49%). In an alternative procedure, t-butylmercaptan (500g) was added drop-wise over 6½ hours to a slurry of sodium hydride (80% dispersion in oil, 163g) in dry diglyme (2.22 litres) under an atmosphere of nitrogen. The reaction was exothermic and the rate of addition was set to hold the temperature below 40°C. A white suspension formed which thickened as the reaction progressed. After stirring overnight, the suspension was diluted with a further 400mls of diglyme and cooled to 0–5°C. A solution of 1,3-dichloro-acetone in diglyme (710mls) was then added drop-wise over a period of 6 hours. The reaction mixture was allowed to warm up to room temperature over 1 hour and then methanol (50mls) was added to destroy excess sodium hydride. The resultant mixture was partitioned between water (4 litres) and toluene (3 litres). The aqueous layer was back-extracted with toluene (2 litres) and the combined organic layers were washed with water (2×3 litres), dried and concentrated *in vacuo* to afford 1,3-di(*t*-butylthio)acetone (VII, $R^1=R^2=t$-Bu—see Scheme 2) (570g, 88%) which could if desired be used in the next stage of the synthesis without further purification.

To a solution of 1,3-di(*t*-butylthio)acetone (25g) in sodium-dried diethyl ether (150ml) at room temperature was added a solution of benzylamine (29.8g) in sodium-dried diethyl ether (50ml). After 1 hour, titanium tetrachloride (10.1g) was added slowly and stirring was continued at room temperature for a further 3 hours. The resultant mixture was filtered through celite and the solvent removed *in vacuo* afford the benzylimine of 1,3-di(*t*-butylthio) acetone (VI-B, X=Bz,$R^1=R^2=t$-Bu—see Scheme 2) as a brown oil (23.07g) which was used immediately in the next stage of the synthesis without further purification.

To a solution of oxalyl chloride (8.91g) in dry dichloromethane (300ml) at 50°C was added a solution containing the benzylimine of 1,3-di(*t*-butylthio)acetone (22.7g) and triethylamine (7.1g) in dry dichloromethane (600ml). The mixture was stirred for 2 hours, allowed to warm up to room temperature and then washed with water, sodium bicarbonate solution and saturated brine. The organic phase was dried over sodium sulphate, filtered and evaporated to give a brown oil. Trituration with petrol followed by chromatography of the residue on silica (eluent: dichloromethane-diethyl ether mixtures) afforded compound (V, X=Bz $R^1=R^2=t$-Bu—see Scheme 1) as a brown solid (14.8g, 56%, m.p. 158°C.

Compound (V, X=Bz,$R^1=R^2=t$-Bu—see Scheme 1) (1.4g) and ammonium acetate (2.86g) were ground together into a fine powder and then fused at *ca* 140°C for 2 hours. The mixture was allowed to cool and then taken up into dichloromethane. The organic phase was basified with sodium bicarbonate solution, washed with water and brine, and the dried over anhydrous magnesium sulphate. The resultant solution was filtered through a silica plug (eluent-diethylether) to afford, after evaporation, compound (IV, X=Bz, Y=H, $R^1=R^2=t$-Bu—Scheme 1) as a brown

solid (1.27g 91%), m.p. 119–120°C.

To a solution of (IV; X=Bz, Y=H $R^1=R^2=t$-Bu—see Scheme 1) (1.0g) in sodium-dried tetrahydrofuran (50ml) was added methoxyacetyl chloride (0.57g). The resultant solution was stirred at room temperature for 16 hours. The tetrahydrofuran was evaporated off and replaced by dichloromethane. The resultant solution was washed with sodium bicarbonate solution and dried over anhydrous magnesium sulphate. Filtration through a silica plug (eluent-diethyl ether) gave compound (III, X=Bz, Y=H, $Z=CH_2OCH_3$, $R^1=R^2=t$-Bu—see Scheme 1) as an oil (0.87g, 73%), ($CDCl_3$) 1,37 (18H); 3.48 (3H,S); 4.04 (2HS); 5.22 (2H,S); 6.80 (1H,S); 7.25 (5H, n); 8.18 (1H,br.s).

To a solution of compound (II, X=Bz, Y=H, $Z=CH_2OCH_3$, $R^1=R^2=t$-Bu) (0.85g) in trifluoroacetic acid (20ml) was added mercury (II) acetate (0.60g). The resultant solution was stirred at room temperature for one hour and the trifluoracetic acid then removed by evaporation *invacuo*. The solid residue was redissolved in *N, N*-dimethylformamide (20ml) and treated with hydrogen sulphide at room temperature for two hours. Nitrogen was then bubbled through the reaction mixture to remove traces of hydrogen sulphide and the black suspension was filtered through celite. A solution of iodine (0.48g) in chloroform (20ml) was added at room temperature and the solution stirred at room temperature for thirty minutes. The solvents were removed by evaporation *in vacuo*, and the residue was separated on silica (eluent diethyl ether) to afford 6-(methoxyacetylamino)-4-benzyl-1,2-dithiolo[4,3-b] pyrrol-5(4H)-one (Compound No. 13 of Table I) as a yellow solid. (408mg, 64%), m.pt. 96–98°C, ($CDCl_3$) 3.49 (3H,S); 4.02 (2H,S); 4.99 (2H,S); 6.48 (1H,S); 7.26 (5H, M); 8.50 (1H,br.s); m/e 334 (M^+), 289, 275, 261, 241, 91, 45.

EXAMPLE 2

An emulsifiable concentrate was made up by mixing the ingredients, and stirring the mixture until all the constituents were dissolved.

Compound of Example 1	10%
Ethylene dichloride	40%
Calcium dodecylbenzenesulphate	5%
"Lubrol" L	10%
"Aromasol" H	35%

EXAMPLE 3

A composition in the form of grains readily dispersible in a liquid, eg. water, was prepared by grinding together the first three ingredients in the presence of added water and then mixing in the sodium acetate. The resultant mixture was dried and passed through a British Standard mesh sieve, size 44–100, to obtain the desired size of grains.

Compound of Example 2	50%
"Dispersol" T	25%
"Lubrol" APN5	1.5%
Sodium acetate	23.%

EXAMPLE 4

The ingredients were all ground together to produce a powder formulation readily dispersible in liquids.

Compound of Example 3	45%
"Dispersol" T	5%
"Lissapol" NX	0.5%
"Cellofas" B600	2%
Sodium acetate	47.5%

EXAMPLE 5

The active ingredient was dissolved in a solvent and the resultant liquid was sprayed on to the granules of China clay. The solvent was then allowed to evaporate to produce a granular composition.

Compound of Example 4	5%
China clay granules	95%

EXAMPLE 6

A composition suitable for use as a seed dressing was prepared by mixing the three ingredients.

Compound of Example 5	50%
Mineral oil	2%
China clay	48%

EXAMPLE 7

A dusting powder was prepared by mixing the active ingredient with talc.

Compound of Example 6	5%
Talc	95%

EXAMPLE 8

A Col formulation was prepared by ball-milling the constituents set out below and then forming an aqueous suspension of the ground mixture with water.

Compound of Example 7	40%
"Dispersol" T	10%
"Lubrol" APN5	1%
Water	

EXAMPLE 9

A dispersible powder formulation was made by mixing together the ingredients set out below and then grinding the mixture until all were thoroughly mixed.

Compound of Example 8	25%
"Aerosol" OT/B	2%
"Dispersol" A.C.	5%
China clay	28%
Silica	40%

EXAMPLE 10

This Example illustrates the preparation of a dispersible powder formulation. The ingredients were mixed and the mixture then ground in a comminution mill.

Compound of Example 9	25%
"Perminal" BX	1%
"Dispersol" T	5%
Polyvinylpyrrolidone	10%
Silica	25%
China clay	34%

EXAMPLE 11

The ingredients set out below were formulated into a dispersible powder by mixing then grinding the ingredients.

Compound of Example 10	25%
"Aerosol" OT/B	2%
"Dispersol" A	5%
China clay	68%

In Examples 2 to 11 the proportions of the ingredients given are by weight. The remaining compounds of Table I were all similarly formulated as per Examples 2 to 11.

There now follows an explanation of the compositions or substances represented by the various Trade Marks and Trade Names mentioned above.

LUBROL L :	a condensate of nonyl phenol (1 mole) with ethylene oxide (13 moles)
AROMASOL H :	a solvent mixture of alkylbenzenes
DISPERSOL T & AC :	a mixture of sodium sulphate and a condensate of formaldehyde with sodium naphthalene sulphonate
LUBROL APN5 :	a condensate of nonyl phenol (1 mole) with naphthalene oxide (5.5 moles)
CELLOFAS B600 :	a sodium carboxymethyl cellulose thickener
LISSAPOL NX :	a condensate of nonyl phenol (1 mole) with ethylene oxide (8 moles)
AEROSOL OT/B :	dioctyl sodium sulphosuccinate
PERMINAL BX :	a sodium alkyl naphthalene sulphonate

EXAMPLE 12

The compounds were tested against a variety of mainly foliar fungal diseases of plants. The techniques employed were as follows.

For all tests the plants were grown in John Innes Potting Compost (No. 1 or 2) in 4 cm diameter minipots. The test compounds were formulated either by bead milling with aqueous Dispersol T or as a solution in acetone or acetone/ethanol which was diluted to the required concentration immediately before use. The solutions or suspensions (100 ppm ai.) were sprayed on the foliage and applied to the roots of the plant via the soil. The sprays were applied to maximum retention and the root drenches to a final concentration equivalent to approximately 40 ppm ai./dry soil. Tween 20, to give a final concentration of 0.05%, was added when the sprays were applied to cereals. (ai. means "active ingredient").

Most were protectant tests where the compound was applied to the soil and roots and to the foliage one or two days before the plant was inoculated with the pathogen.

The foliar pathogens were applied by spraying as spore suspensions onto the leaves of the test plants.

After inoculation, the plants were placed in an appropriate environment to allow infection to proceed and then incubated until the disease was ready for assessment. The period between inoculation and assessment varied from four to fourteen days according to the disease and the environment.

Disease control was recorded using the following grading system :

4=no disease
3=trace to 5% of disease on untreated plants
2=6–25% of disease on untreated plants
1=26–59% of disease on untreated plants
0=60–100% of disease on untreated plants

The results are shown in Table II.

TABLE II

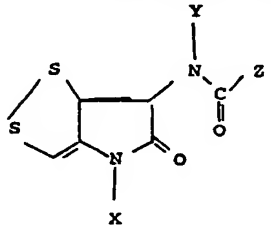
COMPOUND NUMBER	PUCCINIA RECONDITA (WHEAT)	VENTURIA INAEQUALIS (APPLES)	PIRICULARIA ORYZAE (RICE)	CERCOSPORA ARACHIDICOLA (PEANUTS)	PLASMOPARA VITICOLA (VINES)
1	0	4	3	0	3
2	0	ND	0	ND	3
3	0	ND	3	0	4
4	3	o	2	1	3
5	1	0	0	3	3
6	0	4	0	3	4
7	4	0	0	0	4
8	0	0	0	4	4
9	4	4	3	0	4
10	2	4	3	1	4
11	0	0	0	1	0
12	3	3	2	0	2
13	3	3	0	3	3
14*	2	3	0	1	4
16*	0	0	0	ND	2
17	0	4	0	4	4
18	4	4	2	2	4
19*	0	0	0	0	1
22	0	0	0	0	1
27	3	4	0	0	4
28	3	0	0	0	4

ND - NO DATA
* _ 25ppm FOLIAR SPRAY ONLY

MJR/jlw PP 33359
1st Dec 85

CLAIMS

1. A compound having the general formula (I) :



(I)

wherein X, Y and Z, which may be the same or different, are optionally substituted alkyl, cycloalkyl, aryl, aralkyl, alkenyl or a heterocyclic group;
or a hydrogen atom;
or wherein Z is alkoxycarbonyl provided that when Y is a hydrogen atom, X is not methyl or a hydrogen atom; and further provided that when Y is methyl, X is not a hydrogen atom.

2. A compound according to claim 1 wherein one or more of X, Y and Z is an alkyl group containing from 1 to 6 carbon atoms which is either unsubstituted or is substituted by one or more halogen atoms, or wherein one or more of X, Y and Z is a cyclopropyl, cyclobutyl, cyclo pentyl or cyclohexyl group.

3. A compound according to claim 2 wherein the alkyl group contains from 1 to 4 carbon atoms.

4. A compound according to claim 1 wherein one or more of X, Y and Z is an alkenyl group containing from 3 to 6 carbon atoms.

5. A compound according to claim 1 wherein one or more of X, Y or Z is an aralkyl, aralkenyl or aryl group optionally substituted by one or more of halogen, haloalkyl, alkyl, alkoxy, optionally substituted phenyl and optionally substituted phenoxy.

6. A compound according to claim 5 wherein one or more of X, Y or Z is a phenyl group or a benzyl group or an allylphenyl group optionally substituted in the benzene ring by one or more of halogen, C_{1-4} alkyl, halo C_{1-4} alkyl, phenyl, or phenoxy.

7. A compound according to claim 1 wherein X is C_{1-4} alkyl, benzyl, phenyl, C_{1-4} alkoxy phenyl, or allyl;

8. A compound according to claim 1 or claim 7 wherein Y is hydrogen, methyl or phenyl;

9. A compound according to claim 1, 7 or 8 wherein Z is $C1_{-5}$ alkyl optionally substituted by fluorine or chlorine or by methoxy; methoxy or ethoxy carbonyl, 3-phenylall-1-yl.

10. A process for the manufacture of a compound claimed in claim 1 which comprises any of the reaction sequences 1 to 4 herein set forth; or any part of, or combination of, these reaction sequences; or any individual step thereof.

11. Compounds having the formula (VIII) or (IV) wherein R^1 and R^2, which may be the same or different, are alkyl or aralkyl groups and X and Y are as defined in any of claims 1 to 9.

12. Compounds according to claim 11 wherein R^1 and R^2 are a *t*-butyl group.

13. A fungicidal composition comprising a compound according to any of claims 1 to 9 and a carrier or diluent.

14. A method of combating fungi, which comprises applying to a plant, to a seed of a plant, or to the locus of the plant or seed, a compound according to any of claims 1 to 9 or a composition according to claim 13.

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